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CASE REPORT

Long-term effects of COVID-19 in a patient on maintenance dialysis

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Abstract

Coronavirus infectious disease (COVID-19) is a novel respiratory infection highly associated with severe complications in elderly subjects affected by cardiovascular disease. Patients on maintenance dialysis are exceptionally vulnerable because most of them are old and have multiple comorbidities. We report the complex clinical course of SARS-CoV-2 infection in a patient on maintenance dialysis who presented with fever and lung edema. After 41 days from the primary infection, the clinically recovered patient experienced symptomatic reactivation of SARS-COV-2 infection documented by positive polymerase chain reaction (PCR) result on nasal/oropharyngeal swab along with immunoglobulin M seroconversion. The recurrence of PCR positivity forced us to perform hemodialysis in a separate isolation room for a prolonged period of time. Close monitoring of previously infected patients and restructuring of dialysis facilities are necessary to avoid new outbreaks of this concerning disease.

Keywords: COVID, SARS-CoV, coronavirus, dialysis, reactivation

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INTRODUCTION

Coronavirus infectious disease (COVID-19) is an emerging and concerning viral infection, spreading globally from December 2019. The infection principally involves the respiratory tract and manifests with atypical pneumonia, evolving in acute respiratory distress syndrome and sepsis in the most severe form.[1] There is little information about the outcome of patients with chronic kidney disease.[2-7] Patients on renal replacement therapy are the most vulnerable for SARS-CoV-2 infection, as they are old and have a high burden of multiple comorbidities. We report clinical manifestation and outcome of COVID-19 in a patient on maintenance dialysis with long-term infection due to recurrent polymerase chain reaction (PCR) positivity and recrudescence of COVID-19 after clinical and laboratory resolution of the disease.

Case presentation

A 72-year-old man, on peritoneal dialysis (PD) from November 2017 for end-stage renal disease due to chronic interstitial nephritis, was admitted in March 2020 for acute pulmonary edema.

His medical history included diabetes type II, hypertension, coronary artery disease, and atrial fibrillation. He was on continuous ambulatory PD (CAPD) with three diurnal exchanges of 2 L per dwell and an overnight dwell with 1.5 L of icodextrin; diuresis accounted for 700 mL daily.

On admission (4 March 2020) he presented with dyspnea, fever (38.5°C–101.3°F) and hypoxemia (PaO_2, 43 mmHg; PaO_2/FiO_2, 166.5). He was on empirical antibiotic treatment with amoxicillin and clavulanic acid for endodontic abscess.

Physical examination revealed bilateral diffuse crackles. The patient had normal arterial blood pressure (139/68 mmHg) and regular heart beating rate. Bodyweight was 2 kg above the ideal weight (88 vs. 86 Kg). Chest x-rays showed diffuse bilateral pulmonary opacities with heart enlargement (Figure 1A).

Lab examinations showed normal white cell count and C-reactive protein (CRP) level. Initial therapy with oxygen therapy (6 L/min), a bolus injection of furosemide (100 mg) and short exchange with hypertonic dialysate solution (3.86%) prompted slight relief of dyspnea and reduction of the need for oxygen to 3 L/min (oxygen saturation, 94%). Lung edema was managed with continuous intravenous furosemide (250 mg daily), and short exchanges with hypertonic dialysate solution.

On day 7 after admission, for the persistence of low-grade fever (37.5°C–99.5°F), cough, and sore trout, despite the lack of signs of infection (CRP of 0.6 mg/dL) and microbial identification from blood and urine culture, we performed nasal/oropharyngeal swabs for SARS-CoV-2 that yielded a positive result. Chest x-ray revealed patchy ground-glass opacities compatible with atypical pneumonia (Figure 1B). We did not administer antiviral agents or hydroxychloroquine for the progressive improvement of respiratory function and the disappearance of fever.

On day 9 after admission, the patient was dismissed at home, apyretic, and with a normal blood oxygen level

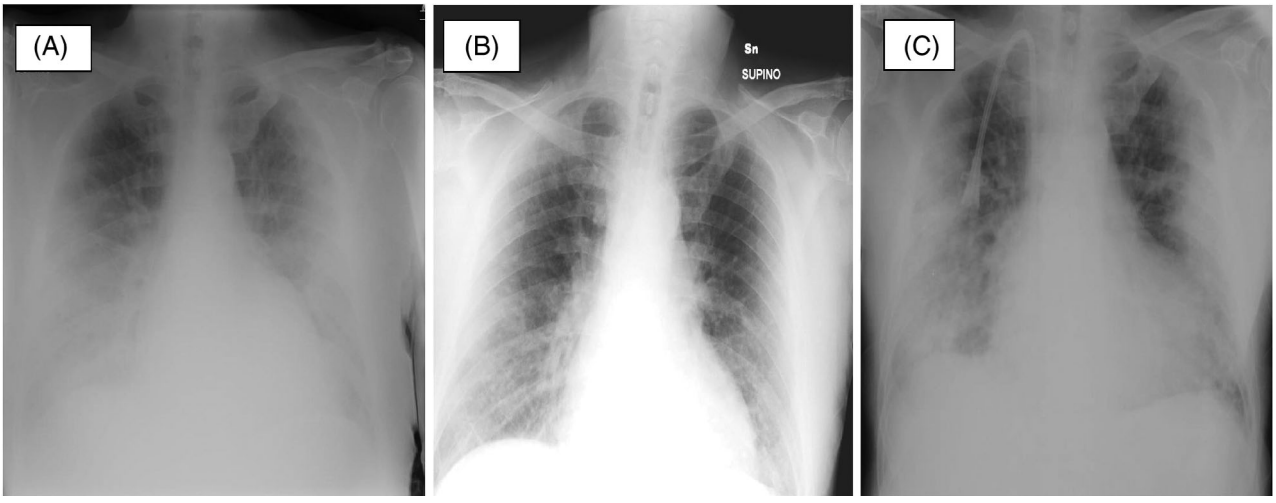

Figure 1 Chest x-ray. (A) Extensive bilateral airspaces disease and cardiomegaly. (B) Partial reduction of lung vascular congestion and bilateral pleural effusion; detection of ground-glass opacities in both basal fields. (C) Detection of consolidative opacities in both lung fields.

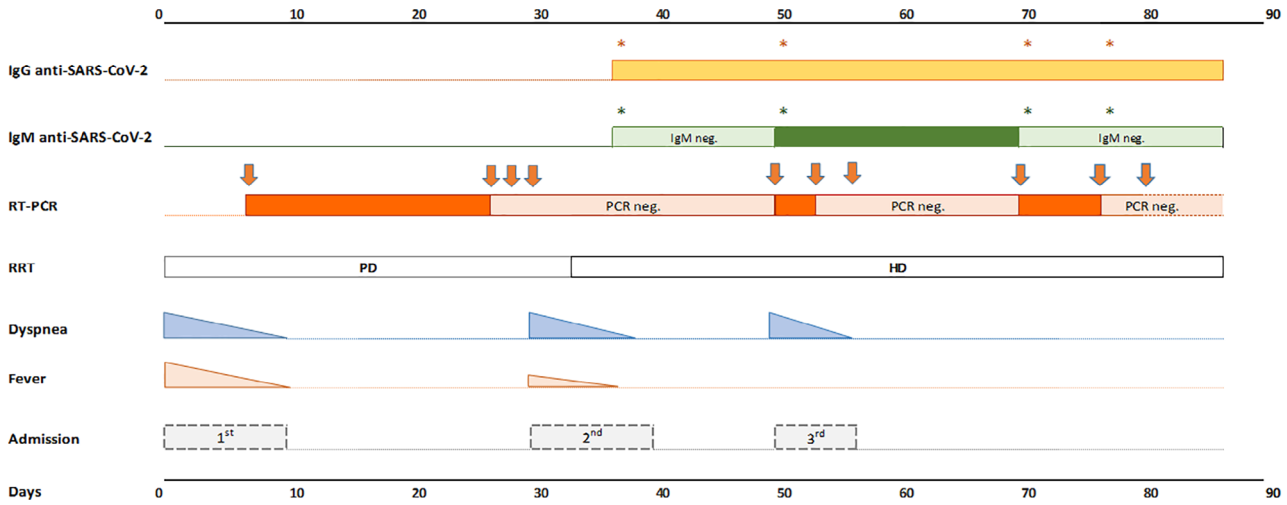

Figure 2 Graphical representation of patient's clinical course from the presentation of the symptoms to the apparent resolution of the infection. Asterisk denotes serologic test; arrow denotes nasal/oropharyngeal swab. [Color figure can be viewed at wileyonlinelibrary.com]

(pO_2, 78.3 mmHg; PaO_2/FiO_2, 372.8), where he continued CAPD program in self-isolation. Here, the patient recovered from SARS-CoV-2 as documented by three negative nasal/oropharyngeal specimens.

On day 28 from the onset of the COVID-19 symptoms, the patient was newly admitted for lung edema due to fluid overload and low-grade fever. He started antibiotic therapy for a progressive increase of serum procalcitonin level. Blood culture and RT-PCR for respiratory viruses in the gargle specimen resulted negative. Nasal/oropharyngeal PCR for SARS-CoV-2 resulted negative and serological testing showed positive anti-SARS-CoV-2 immunoglobulin G (IgG). Given the progressive reduction of diuresis PD was switched to hemodiafiltration to maintain the ideal body weight.

On day 48 days from the first presentation and 41 day from the diagnosis of COVID19, the patient was admitted for the third time for dyspnea (30 breaths per minute), hemoptysis, hypoxia (PO_2, 52 mmHg; PO_2/FiO_2, 250) and multiple bilateral lung opacities at chest x-rays (Figure 1C). A positive nasal/oropharyngeal swab for SARS-CoV-2 along with immunoglobulin M (IgM) seroconversion was consistent with recrudescence of SARS-CoV-2 infection (Figure 2). The search for SARS-CoV-2 on peritoneal effluent provided a negative result. Respiratory function gradually improved without antibiotic therapy. The reduction of the ideal body weight of 4 kg leads to a rapid resolution of the respiratory symptoms. He was discharged home on day 7 from admission with a negative PCR result on the oropharyngeal/nasal swab. He continued alternate-day dialysis to avoid fluid overload. On day 79 from the onset of COVID-19 symptoms, nasal/oropharyngeal swab yielded a second negative result after the third-positive test. Compared with anti-SARS-CoV-2 IgG, IgM were charactherized by an early disapparence from serum; indeed, they were detected for only 20 days.

DISCUSSION

This case describes the complex clinical course of a patient on maintenance dialysis with presenting symptoms compatible with recrudescence of COVID-19 and prolonged positivity of PCR on nasal/oropharyngeal swabs.

To date, there are few data about the impact of this infection on subjects on maintenance dialysis. In Wuhan, the epicenter of the outbreak, two case-series have been described with different findings in terms of prevalence and outcome. In one center, 37 out of 230 (16%) hemodialysis (HD) patients contracted the infection and six (16%) died.[5] In the other HD center, 5 out of 201 (2.48%) HD patients resulted infected by SARS-CoV-2 infection and no one died at the end of the study period.[6] In a large HD facility in Northern Italy, the prevalence of infection was 5.21% with a fatality rate of 23.8%.[3] In the city of Modena (Northern Italy), we recorded six fatal infections (mortality rate of 40%) among 280 patients on maintenance dialysis.[7]

The clinical course of this concerning infectious disease appears unpredictable and associated with a variable

fatality rate. The outcome of the disease relies on a complex interplay between the pathogenicity of the virus and the host immune response. Once recovered from the infection, there is uncertainty about the modalities of surveillance and interpretation of the serologic tests. It is unclear if antibodies that result from SARS-CoV-2 infection are able to provide immunity for future infection. Moreover, there is a lack of knowledge about the major determinant of humoral immunity including the titer of antibodies required for protection, the duration of protection, and the factors associated with the development of a protective host immune response antibody response.

The "recrudescence" of symptoms and signs of COVID-19 and PCR positivity for SARS-CoV-2 in a patient with IgG antibodies raises many questions on the clinical course of the disease and the ability of the patients on maintenance dialysis in controlling the infection. We are unable to determine precisely if the recurrence of COVID-19 is due to "reinfection" or "reactivation" of the virus. The clinically resolved infection along with negative PCR results of three nasal/oropharyngeal specimens, performed within 41 days from primary infection, supported the possibility of reinfection and excluded the recrudescence of the disease due to the viral persistence in the upper respiratory tract.

In our case, the recurrence of the disease was clinically evident, as witnessed by the severe lung involvement requiring in-hospital care and simultaneous IgM seroconversion. The fast resolution of the respiratory symptoms, in part due to the resolution of volume overload, and the rapid clearance of the virus determined a milder clinical course than the primary infection. The evolution of the disease was coherent with the definition of reinfection[8] which defines this condition as asymptomatic, and, if symptomatic, it presents with milder symptoms than the primary infection.

Immune response has a central role in the occurrence of the reinfection, but the lack of knowledge about the immune mechanism (humoral or cell-mediated) involved in the clearance of SARS-CoV-2 limits our current understanding of the virus pathogenicity. Waning immunity, due to the state of renal failure, re-challenge with a high viral load, the persistence of low-level viremia in the lower respiratory tract (viral reactivation), or infection with a new viral strain (rare) are all attractive hypotheses that highlight the "partial" neutralizing effect of IgG antibodies against SARS-CoV-2.

The prolonged period of viral shedding opens important clinical questions on the correct management of patients on maintenance HD. There is consensus that a prolonged course of the disease generally occurs in a subject with severe symptoms.[9] In a cohort of Chinese patients, the median time of viral shedding persistence was 20 days and the longest duration of viral shedding in survivors was 37 days.[10] Many authors support the thesis that positive RT-PCR results can occur with the detection of small fragments of the virus on the nasal mucosa.[11] In the absence of viral cultures assay able to identify viral replication and hence, virus infectivity, all containment measures to avert virus spreading are necessary for the dialysis facilities. A profound reorganization of the places used to perform renal replacement therapy must ensure the correct isolation of infected patients. Potentially infected patients awaiting molecular results and patients with a negative RT-PCR result but with not reassuring serological pattern (IgM positive and IgG negative) should be placed in a separate isolation room. Overall, each dialysis facility should identify at least three zones to deliver the best standard of care. They should be dedicated to infected, potential infected, and not-infected patients. To prevent the spread of the virus among patients and health care workers, our current strategy consists to perform a third nasal/oropharyngeal swabs 14 days after the resolution of the infection before reinstating the patients among healthy subjects.

CONCLUSION

Long-term infectivity of SARS-CoV-2 force nephrologists to operate careful surveillance in clinically recovered patients on maintenance dialysis to prevent and control outbreaks.

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STATEMENT OF ETHICS

This study complies with the guidelines for human studies and include evidence that the research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Ethical committee "Comitato Etico dell'Area Vasta Emilia Nord" of the "Azienda Ospedaliero-Universitaria di Modena" approved this study (protocol number: AOU 0010159/20).

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